L5 ANSWER 31 OF 33 MEDLINE
AN 84131815 MEDLINE
DN 84131815
TI Differential biological activities between mono- and bivalent fragments of anti-prolactin receptor antibodies.
AU Dusanter-Fourt I; Djiane J; Kelly P A; Houdebine L M; Teyssot B
SO ENDOCRINOLOGY, (1984 Mar) 114 (3) 1021-7.
Journal code: EGZ. ISSN: 0013-7227.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198406
AB Previous studies have established that antibodies against PRL receptors can mimic PRL effects on casein gene expression and on thymidine incorporation into DNA in the mammary gland. In the present work, bivalent F(ab')2 and monovalent Fab' fragments of the anti-PRL receptor antibodies were prepared. Both inhibited the binding of 125I-labeled PRL to rabbit mammary gland membranes. F(ab')2 as well as the unmodified antibodies were able to enhance casein synthesis and thymidine incorporation into DNA in cultured rabbit mammary gland explants. Moreover, when added to isolated membranes, both were able to induce the generation of the PRL relay which specifically stimulates caseins gene transcription in isolated mammary nuclei. In contrast, monovalent fragments were totally devoid of any of these PRL-like activities. However, bivalent and monovalent antibodies were equipotent in inducing a down-regulation of PRL receptors in mammary explants. These data indicate that the biological PRL-like activity of antibodies against PRL receptors is strictly related to their **bivalent structure**. This fact indicates a possible crucial role of a microaggregation of PRL receptors in the transmission of the PRL message across the membranes. In addition, these experiments reinforce the idea that internalization and down-regulation are not directly related to PRL action on casein or DNA synthesis in mammary gland.
CT Check Tags: Animal; Female
Antigen-Antibody Complex
*Autoantibodies
Caseins: ME, metabolism
DNA Replication
Immunoglobulins, Fab
Kinetics
*Mammae: ME, metabolism
Organ Culture
*Prolactin: ME, metabolism
Pseudopregnancy
Rabbits
Receptors, Cell Surface: IM, immunology
*Receptors, Cell Surface: ME, metabolism
RN 9002-62-4 (Prolactin)
CN 0 (Antigen-Antibody Complex); 0 (Autoantibodies); 0 (Caseins); 0 (Immunoglobulins, Fab); 0 (Receptors, Cell Surface); 0 (Receptors, Prolac

5 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2001 ACS
AN 1993:116902 CAPLUS
DN 118:116902
TI Drug design of neuropeptides for hypotensive therapeutics
AU Shimohigashi, Yasuyuki; Matsumoto, Hiroshi; Sakaguchi, Kazuyasu
CS Fac. Sci., Kyushu Univ., Fukuoka, 812, Japan
SO Kenkyu Hokoku - Asahi Garasu Zaidan (1992), Volume Date 1991, 59, 115-24
CODEN: KHAZE2
DT Journal
LA Japanese
CC 2-2 (Mammalian Hormones)
AB Three dimeric analogs of substance P (SP1-11), D-SP1-11 (-CH2O-Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH2)2, D-SP2-11, and D-SP3-11, were synthesized together with their monomeric derivs. These 3 analogs showed selective binding to the tachykinin receptor subtype NK-1. D-SP1-11 showed the strongest depression of blood pressure, and its tonic effect was superior to that of other analogs. An extreme stability of D-SP1-11, as compared with its monomeric analogs, was shown in blood plasma. The vascular tachykinin receptors might have a **bivalent structure** to which D-SP1-11 can fit specifically.
ST substance P analog hypotensive
IT Antihypertensives
(substance P dimeric analogs as)
IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuropeptides, hypotensive activity of)
IT 33507-63-0D, Substance P, dimeric analogs 146321-30-4 146321-31-5 146342-97-4
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hypotensive activity of)

13 ANSWER 5 OF 5 MEDLINE
AN 95174765 MEDLINE
DN 95174765
TI Inhibition of T cell activation with a humanized anti-beta 1 integrin chain mAb.
AU Poul M A; Ticchioni M; Bernard A; Lefranc M P
CS Laboratoire d'ImmunoGenetique Moleculaire, LIGM, UMR 9942, CNRS, Universites Montpellier I et II, France.
SO MOLECULAR IMMUNOLOGY, (1995 Feb) 32 (2) 101-16.
Journal code: NG1. ISSN: 0161-5890.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-S77020; GENBANK-S77022
EM 199506
AB The murine anti-CD29 mAb K20 (Mu-K20) is known to bind to the beta 1 chain of the human integrins and to inhibit activation and proliferation of T cells, implying an important potential for in vivo immunosuppression. However, use of K20 as an immunosuppressant drug would be impaired by the immunogenicity of mouse mAbs in man. We have therefore **engineered** K20 into (1) a mouse/human chimeric mAb (Ch-K20) that comprises the human kappa/gamma 1C regions and the K20 V regions; and (2) a humanized mAb (Hu-K20) combining the complementarity-determining regions (**CDRs**) of the K20 mAb with human framework (**FR**) and kappa/gamma 1 C regions. Both chimeric and humanized Abs were able to reproduce a range of functional properties of the original mouse mAb K20 (Mu-K20), namely, specific binding of CD29, inhibition of T cell proliferation and elevation of second messenger phosphatidic acid (PA) induced via CD3 in a soluble form, and activation of T cell proliferation in a cross-linked form. When compared to Ch-K20, the avidity of Hu-K20 was only slightly reduced. This demonstrates the feasibility of a successful humanization performed on the sole basis of the primary amino acid sequence analysis of the original mouse antibody V regions.
CT Check Tags: Animal; Human; Support, Non-U.S. Gov't
Amino Acid Sequence
Antibodies, Monoclonal: BI, biosynthesis
*Antibodies, Monoclonal: IM, immunology
Antigens, CD: IM, immunology
Base Sequence
Binding, Competitive
Chimeric Proteins: BI, biosynthesis
*Chimeric Proteins: IM, immunology
Cloning, Molecular
Complement 1q: IM, immunology
Cytotoxicity Tests, Immunologic
Gene Rearrangement, B-Lymphocyte: GE, genetics
Hybridomas: IM, immunology
Immunoglobulins, kappa-Chain: GE, genetics
Immunoglobulins, Fab: IM, immunology
Immunoglobulins, Heavy-Chain: GE, genetics
*Integrins: IM, immunology
*Lymphocyte Transformation: IM, immunology
Mice
Molecular Sequence Data
Phosphatidic Acids: BI, biosynthesis
*T-Lymphocytes: IM, immunology
RN 80295-33-6 (Complement 1q)
CN 0 (Antibodies, Monoclonal); 0 (Antigens, CD); 0 (Antigens, CD29); 0 (Chimeric Proteins); 0 (Immunoglobulins, kappa-Chain); 0 (Immunoglobulins, Fab); 0 (Immunoglobulins, Heavy-Chain); 0 (Integrins); 0 (Phosphatidic Acids)
GEN V.kappa.; VH

16 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2001 ACS
AN 1992:5189 CAPLUS
DN 116:5189
TI Oligomeric monoclonal immunoglobulins for immunodiagnosis and therapy
IN Shuford, Walt W.; Harris, Linda J.; Raff, Howard V.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-14
ICS A61K039-00; A61K039-40; C12N005-02; C12N015-00
CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9106305	A1	19910516	WO 1990-US6426	19901106
W: AU, CA, FI, JP, KR, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2045150	AA	19910508	CA 1990-2045150	19901106
AU 9170303	A1	19910531	AU 1991-70303	19901106
AU 648056	B2	19940414		
EP 462246	A1	19911227	EP 1991-901546	19901106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 04505709	T2	19921008	JP 1991-501918	19901106
NO 9102640	A	19910905	NO 1991-2640	19910705
PRAI US 1989-432700	19891107			
WO 1990-US6426	19901106			

AB Oligomeric monoclonal **antibodies** with high avidity for **antigen** are prepd. that have .gtoreq.2 Ig monomers assocd. together to form tetravalent or hexavalent Ig, esp. IgG. The oligomers are formed by substantially duplicating regions of the **light chain**, particularly the variable region. Oligomeric **antibodies** of the IgG isotype cross the placenta and can provide passive immunity to a fetus, which is particularly important for protecting newborns against, e.g. group B streptococci. A monoclonal antibody having a mol. wt. substantially greater than a typical IgG antibody was produced using V region genes cloned from the parental 4B9 lymphoblastoid cell line. The antibody (1B1 dimer) was specific for group B streptococcus, was 100-fold more active in an opsonophagocytic assay than the monomer, and passed through the placenta and into the fetus of rats. Rat pups treated with the antibody after i.p. injection of streptococci were protected at both low and high concns. of antibody. DNA sequences are shown for the 1B1 **light chain** and for chains of the 4B9 antibody.

ST oligomer monoclonal Ig diagnosis therapy; IgG oligomer Streptococcus newborn immunization; cloning IgG oligomer prodn

IT Mammal
(cell line of, oligomeric monoclonal Ig secretion by)

IT Phagocytosis
(enhancement of, with oligomeric monoclonal IgG)

IT Gene, animal
RL: PREP (Preparation)
(for Ig, cloning of, in prepn. of oligomeric monoclonal Ig for diagnosis and therapy)

IT Molecular cloning
(of genes for Ig, in prepn. of oligomeric monoclonal Ig for diagnosis and therapy)

IT **Polymerization**
(of monoclonal Ig, amino acid substitution for, in prodn. of oligomeric monoclonal Ig for immunodiagnosis and therapy)

IT Pharmaceutical dosage forms
(of oligomeric monoclonal IgG)

IT Animal cell line
(oligomeric monoclonal Ig secretion by)

IT Placenta
(oligomeric monoclonal Ig transport across, for passive immunization of fetus)

IT **Antigens**
RL: BIOL (Biological study)

(substitution of, in Ig **light chain**, in prodn. of oligomeric monoclonal Ig for immunodiagnosis and therapy)

IT Animal cell line
(4B9, oligomeric monoclonal Ig derived from)

IT Immunoglobulins
RL: PREP (Preparation)
(G, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)

IT Immunoglobulins
RL: PREP (Preparation)
(G1, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)

IT Immunoglobulins
RL: PREP (Preparation)
(G2, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)

IT Immunoglobulins
RL: BIOL (Biological study)
(M, oligomeric monoclonal Ig derived from)

IT Embryo
(fetus, passive immunization of, with oligomeric monoclonal Ig)

IT Streptococcus
(group B, passive immunization against, in fetus and newborn, oligomeric monoclonal Ig for)

IT Therapeutics
(immuno-, oligomeric monoclonal Igs for)

IT Diagnosis
(immunol., oligomeric monoclonal Igs for)

IT Immunoglobulins
RL: PREP (Preparation)
(monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)

IT Plasmid and Episome
(pN.gamma.1A2.1, heavy chain of oligomeric monoclonal IgG to group B streptococcus on, cloning and expression of)

IT Immunization
(passive, against streptococci, in fetus and newborn, oligomeric monoclonal Ig for)

IT 137067-93-7 137067-94-8
RL: PRP (Properties)
(amino-terminal sequence of recombinant light Ig chain of 1B1 monoclonal IgG)

IT 137748-88-0, Deoxyribonucleic acid (human clone 4B9-UK15 4B9 immunoglobulin G 1 **light chain** fragment-specifying)
137748-89-1, Deoxyribonucleic acid (human clone 4B9-UK15 immunoglobulin G 1 **light chain** fragment-specifying) 137749-00-9, Deoxyribonucleic acid (human clone pN.gamma.1A2.1 immunoglobulin G 1 heavy chain fragment-specifying) 137749-01-0, Deoxyribonucleic acid (human clone pNkA1.1 immunoglobulin G 1 **light chain** fragment-specifying)
RL: PRP (Properties)
(cloning and nucleotide sequence of)

13 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1992:28050 BIOSIS
DN BA93:17325
TI HUMANIZATION OF A MOUSE MONOCLONAL ANTIBODY BY **CDR**-GRAFTING THE IMPORTANCE OF FRAMEWORK RESIDUES ON LOOP CONFORMATION.
AU KETTLEBOROUGH C A; SALDANHA J; HEATH V J; MORRISON C J; BENDIG M M
CS MED. RES. COUNCIL COLLABORATIVE CENTRE, 1-3 BURTONHOLE LANE, MILL HILL, LONDON NW7 1AD, UK.
SO PROTEIN ENG, (1991) 4 (7), 773-784.
CODEN: PRENE9. ISSN: 0269-2139.
FS BA; OLD
LA English
AB A mouse monoclonal antibody (mAb 425) with therapeutic potential was 'humanized' in two ways. Firstly the mouse variable regions from mAb 425 were spliced onto human constant regions to create a chimeric 425 antibody. Secondly, the mouse complementarity-determining regions (**CDRs**) from mAb 425 were grafted into human variable regions, which were then joined to human constant regions, to create a reshaped human 425 antibody. Using a molecular model of the mouse mAb 425 variable regions, framework residues (**FRs**) that might be critical for antigen-binding were identified. To test the importance of these residues, nine versions of the reshaped human 425 heavy chain variable (VH) regions and two versions of the reshaped human 425 light chain variable (VL) regions were designed and constructed. The recombinant DNAs coding for the chimeric and reshaped human light and heavy chains were co-expressed transiently in COS cells. In antigen-binding assays and competition-binding assays, the reshaped human antibodies were compared with mouse 425 antibody and to chimeric 425 antibody. The different versions of 425-reshaped human antibody showed a wide range of avidities for antigen, indicating that substitutions at certain positions in the human **FRs** significantly influenced binding to antigen. Why certain individual **FR** residues influence antigen-binding is discussed. One version of reshaped human 425 antibody bound to antigen with an avidity approaching that of the mouse 425 antibody.
CC Genetics and Cytogenetics - Animal *03506
Genetics and Cytogenetics - Human *03508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Pharmacology - Immunological Processes and Allergy *22018
Immunology and Immunochemistry - General; Methods *34502
BC Hominidae 86215
Muridae 86375
IT Miscellaneous Descriptors
PROTEIN ENGINEERING GENETICALLY **ENGINEERED** CHEMICAL

L9 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1977:550064 CAPLUS
DN 87:150064
TI Unusual distributions of amino acids in complementarity-determining (hypervariable) segments of heavy and light chains of immunoglobulins and their possible roles in specificity of antibody-combining sites
AU Kabat, Elvin A.; Wu, Tai Te; Bilofsky, Howard
CS Natl. Cancer Inst., NIH, Bethesda, MD, USA
SO Journal of Biological Chemistry (1977), 252(19), 6609-16
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB Using a data bank of sequence of variable regions of immunoglobulin chains to compute incidences of the 20 amino acids at various positions in the **complementarity-detg. segments** of light and heavy chains, it was possible to infer that certain amino acids at 13 positions in the light chain and 7 positions in the heavy chain functioned in antibody-combining sites as structural elements rather than as contacting or conformationally important residues. These inferences are in good agreement with assignments made by x-ray crystallog. in almost all instances. The statistical method, however, is independent of x-ray crystallog. and may permit assigning a role to a position or to a given amino acid at a position in many kinds of antibody-combining sites, while an x-ray structure provides information only about the antibody being studied. The role of individual amino acids at various positions is greatly affected by insertions or deletions in the **complementarity -detg. segments**. The method also permits one to infer that particular amino acids in **complementarity-detg. segments** such as histidine and tryptophan are either directly involved in specificity as contacting residues, or exert a conformational influencee on such residues. The findings indicate the need for x-ray crystallog. studies on immunoglobulins with insertions of different lengths in complmentarity-detg. segments and with sites shown from immunochem. consideration to be grooves or cavities.
ST computer application Ig amino acid; conformation Ig amino acid position; Ig variable sequencee structure site; amino acid distribution complementarity Ig
IT Immunoglobulins
RL: BIOL (Biological study)
(amino acid distribution in complementarity-detg. secments of)
IT **Peptides**, properties
RL: PRP (Properties)
(amino acid sequences of, of Ig, **complementarity-detg . segments** in relation to)
IT Amino acids, biological studies
RL: BIOL (Biological study)
(of Ig, in **complementarity-detg. segments**)
IT 71-00-1, biological studies 73-22-3, biological studies
RL: BIOL (Biological study)
(of Ig, in **complementarity-detg. segments**)

GP501.07 Microfilm.

L13 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1993:140733 BIOSIS
DN PREV199395073533
TI Role of mouse V-H10 and VL gene segments in the specific binding of **antibody** to Z-DNA, analyzed with recombinant single chain Fv molecules.
AU Brigido, Marcelo M.; Polymenis, Michael; Stollar, B. David (1)
CS (1) Dep. Biochem., Tufts Univ. Sch. Med., 136 Harrison Ave., Boston, MA 02111 USA
SO Journal of Immunology, (1993) Vol. 150, No. 2, pp. 469-479.
ISSN: 0022-1767.
DT Article
LA English
AB A plasmid vector was constructed for the expression of a single chain Fv domain of mouse mAb to Z-DNA (**antibody** Z22), which is encoded by V-H10 and V-kappa-10 gene family members along with Dsp2, J-H4, and J-K4 segments. The vector coded for a PhoA secretion signal, VH segment, flexible **peptide linker**, VL segment, (His)-5, and a protein A domain. Unique restriction sites allowed exchange of the segments as cassettes. Bacteria transformed with the vector secreted soluble recombinant Fv with specific Z-DNA-binding activity. When the L chain of Z22 was replaced with a library of splenic VL cDNA from a mouse immunized with Z-DNA, only a light chain closely resembling that of the original Z22 (differing at six amino acid positions) yielded Fv with Z-DNA-binding activity. The Fv with this L chain replacement had a lowered affinity, but remained selective for Z-DNA. Replacement of the Z22 H chain with a mixture of 11 V-H10-encoded H chains yielded two Z-DNA binding clones, but they bound B-DNA and denatured DNA as well as Z-DNA. The replacement clones indicate the importance of the H chain **CDR3** and particular VH-VL combinations in formation of specific **antibodies** to Z-DNA.
CC Genetics and Cytogenetics - Animal *03506
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Immunology and Immunochemistry - General; Methods *34502
BC Muridae *86375
IT Major Concepts
Biochemistry and Molecular Biophysics; Genetics; Immune System (Chemical Coordination and Homeostasis); Methods and Techniques
IT Chemicals & Biochemicals
Z-DNA
IT Sequence Data
amino acid sequence; molecular sequence data
IT Miscellaneous Descriptors
GENETIC ENGINEERING; HEAVY CHAIN; LIGHT CHAIN; REPLACEMENT CLONES; RESTRICTION SITES; VECTOR CONSTRUCTION; Z22 **ANTIBODY**
ORGN Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Muridae (Muridae)
ORGN Organism Superterms
animals; chordates; mammals; nonhuman vertebrates; nonhuman mammals; rodents; vertebrates
RN 121182-96-5 (Z-DNA)

=>

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1980:405826 CAPLUS
DN 93:5826
TI Structural studies of murine lymphocyte surface IgD
AU Goding, James W.
CS Sch. Med., Stanford Univ., Stanford, CA, 94305, USA
SO J. Immunol. (1980), 124(5), 2082-8
CODEN: JOIMA3; ISSN: 0022-1767
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB Lymphocyte surface IgD was labeled with 125I by the lactoperoxidase technique and subjected to cleavage with trypsin or staphylococcal V8 protease. Tryptic cleavage resulted in Fab monomers consisting of one light chain disulfide bonded to an Fd fragment of mol. **wt.** **30,000** and an Fc fragment of mol. **wt.** 60,000, unreduced. Upon redn., the tryptic Fc consisted of one labeled fragment of 16,000 **daltons** when digested to completion. Before completion of digestion, intermediates of 35,000 and **20,** **000 daltons** were obsd. Thus, in addn. to cleavage at the hinge, trypsin causes addnl. cleavages in the Fc, within disulfide loops. Cleavage with staphylococcal V8 protease resulted in an Fc fragment that consisted of disulfide-bonded **20,000** -dalton subunits (sFc) and Fab' fragments made up of one Fd' fragment (40,000 **daltons**) disulfide bonded to one light chain. The sFc fragment exhibited a marked anodal shift in electrophoretic mobility in the presence of Na deoxy cholate, and a marked cathodal shift in the presence of cetyl tri-Me ammonium bromide. The Fab' fragment showed no such shift. These results indicate that (a) the only inter-heavy chain disulfide bonds are situated within the last two domains, and (b) the C-terminal **20,000** **daltons** of IgD contain a region that is capable of binding detergent and thus of interacting with membrane lipid.
ST lymphocyte IgD structure
IT Lymphocyte
(IgD of surface of, structure of)
IT **Immunoglobulins**
RL: BIOL (Biological study)
(D, of lymphocyte surface, structure of)

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1980:530367 CAPLUS
DN 93:130367
TI In vitro studies of human seminal plasma allergy
AU Kooistra, J. B.; Yunginger, J. W.; Santrach, P. J.; Clark, J. W.
CS Dep. Med., Univ. Wisconsin, Madison, WI, USA
SO J. Allergy Clin. Immunol. (1980), 66(2), 148-54
CODEN: JACIBY; ISSN: 0091-6749
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB A 23-yr-old woman experienced generalized urticaria, angioedema, and respiratory obstruction after intercourse. Reactions increased in frequency and severity over a 2-yr period; sexual exposures were limited to her husband. Fresh, centrifuged seminal plasma samples from 4 donors, including her husband, evoked pos. immediate puncture skin-test reactions in dilns. of 1:100 or 1:1,000; no reactions were seen in normal control males. A borderline elevation in serum IgE antibodies to seminal plasma was noted by the radioallergosorbent test (RAST). However, the patient had elevated IgE antibodies to a partially purified seminal plasma fraction (IV) obtained by Sephadex G-200 gel filtration. Seminal plasma from all 4 donors showed similar allergenic activity when tested in fraction IV RAST inhibition expts. Further in vitro studies have characterized the allergenic components in fraction IV. Allergenic components (pool III) are distinct from acid phosphatase, have an apparent mol. **wt.** range from **20,000** to **30,**
000 daltons, produced multiple bands on isoelec.
focusing with isoelec. points of 6.6, 7.0, and 7.5, and produced multiple bands in polyacrylamide gel electrophoresis, indicating a heterogeneous group of antigens. Comparison of pool III with seminal vesicle secretions and prostatic homogenate via thin-layer isoelectrofocusing revealed protein bands which appeared to be common to all 3 materials. Thus, it remains uncertain as to whether allergenic proteins are derived from seminal vesicle or prostatic secretions. Condom usage by the patient's husband essentially prevented subsequent allergic reactions. However, serum IgE antibodies to fraction IV remained consistently elevated during a 28-mo follow-up period.
ST seminal plasma allergy; allergen seminal plasma characterization
IT Allergens
RL: PROC (Process)
(of seminal plasma, characterization of)
IT Allergy
(to seminal plasma protein)
IT **Immunoglobulins**
RL: BIOL (Biological study)
(E, to seminal plasma proteins)
IT Semen
(p

The use of gene fusions to protein A and protein G in immunology and biotechnology.

Stahl S; Nygren PA

Department of Biochemistry and Biotechnology, Royal Institute of Technology (KTH), Stockholm, Sweden.

Pathologie-biologie (FRANCE) Jan 1997, 45 (1) p66-76, ISSN 0369-8114 Journal Code: OSG

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

JOURNAL ANNOUNCEMENT: 9707

Subfile: INDEX MEDICUS

This **review** describes the use of fusion proteins containing the immunoglobulin-binding domains of staphylococcal protein A (SpA) or the serum albumin-binding regions of streptococcal protein G (SpG), respectively, for various applications in immunology and biotechnology. The **review** will not cover the use of SpA and SpG for the purpose of immunoglobulin purification, but instead focus on other applications. Hundreds of SpA/SpG fusion proteins have been described in publications in the context of recombinant protein production, in a wide variety of host cells, with subsequent affinity purification of the gene product. However, this still constitutes just one area of their use. We will thus cover also other aspects of using SpA and SpG, including strategies to: (i) improve in vitro renaturation schemes for expressed gene products, (ii) enable affinity-assisted folding in vivo of target proteins, (iii) improve the stability to proteolysis of produced recombinant proteins, (iv) prolong the in vivo half-life of therapeutic proteins, (v) facilitate subunit vaccine development and functional cDNA analysis, (vi) select novel receptor variants with new specificities by the use of phage display technology.

2 ANSWER 15 OF 15 MEDLINE
AN 95121810 MEDLINE
DN 95121810
TI Single-chain Fvs.
AU Raag R; Whitlow M
CS Department of Chemistry, University of California at Berkeley 94720..
SO FASEB JOURNAL, (1995 Jan) 9 (1) 73-80. Ref: 47
Journal code: FAS. ISSN: 0892-6638.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 199504
AB Single-chain Fvs (sFvs) are **recombinant antibody fragments** consisting of only the variable light chain (VL) and variable heavy chain (VH) domains covalently connected to one another by a polypeptide linker. Due to their small size, sFvs have rapid pharmacokinetics and tumor penetration in vivo. Single-chain Fvs also show a concentration-dependent tendency to oligomerize. Bivalent sFvs are formed when the variable domains of a sFv disassociate from one another and reassociate with the variable domains of a second sFv. Similar rearrangement and reassociation of variable domains from different sFvs can result in the formation of trimers or higher multimeric oligomers. Each Fv in a bivalent or **multivalent** Fv is composed of the VL domain from one sFv and the VH domain from a second sFv. Modifying linker length or the inclusion of antigen may stabilize the VL/VH interface against rearrangement such that specific multimeric or monomeric forms of sFvs may be isolated. Nuclear magnetic resonance studies have shown that McPC603-derived Fv and sFvs have similar structures, and that the sFv linker is a rapidly moving, highly flexible peptide with a random coil-like structure. In X-ray crystallographic investigations of three different sFvs, linkers have also been found to be disordered. Indirect evidence suggests that a monomeric sFv has been crystallized in one case, and dimeric sFvs in the other two.
CT Check Tags: Human
Amino Acid Sequence
Crystallization
*Immunoglobulin Fragments: CH, chemistry
Immunoglobulin Fragments: ME, metabolism
*Immunoglobulin Variable Region: CH, chemistry
Immunoglobulin Variable Region: ME, metabolism
Macromolecular Systems
Molecular Sequence Data
Nuclear Magnetic Resonance
Recombinant Proteins: CH, chemistry
Recombinant Proteins: ME, metabolism
CN 0 (immunoglobulin Fv); 0 (Immunoglobulin Fragments); 0 (Immunoglobulin Variable Region); 0 (Macromolecular Systems); 0 (Recombinant Proteins)

L2 ANSWER 14 OF 15 MEDLINE
AN 97380304 MEDLINE
DN 97380304
TI New protein engineering approaches to **multivalent** and bispecific antibody fragments.
AU Pluckthun A; Pack P
CS Biochemisches Institut der Universitat Zurich, Switzerland.
SO IMMUNOTECHNOLOGY, (1997 Jun) 3 (2) 83-105. Ref: 174
Journal code: CR0. ISSN: 1380-2933.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199711
EW 19971101
AB Multivalency is one of the hallmarks of antibodies, by which enormous gains in functional affinity, and thereby improved performance in vivo and in a variety of in vitro assays are achieved. Improved in vivo targeting and more selective localization are another consequence of multivalency. We summarize recent progress in engineering multivalency from **recombinant antibody fragments** by using miniantibodies (scFv fragments linked with hinges and oligomerization domains), spontaneous scFv dimers with short linkers (diabodies), or chemically crosslinked antibody fragments. Directly related to this are efforts of bringing different binding sites together to create bispecific antibodies. For this purpose, chemically linked fragments, diabodies, scFv-scFv tandems and bispecific miniantibodies have been investigated. Progress in E. coli expression technology makes the amounts necessary for clinical studies now available for suitably engineered fragments. We foresee therapeutic advances from a modular, systematic approach to optimizing pharmacokinetics, stability and functional affinity, which should prove possible with the new recombinant molecular designs.
CT Check Tags: Animal; Human
Amino Acid Sequence
*Antibodies, Bispecific: CH, chemistry
Antibodies, Bispecific: GE, genetics
*Immunoglobulin Fragments: CH, chemistry
Immunoglobulin Fragments: GE, genetics
Molecular Sequence Data
*Protein Engineering
Recombinant Proteins: CH, chemistry
CN 0 (Antibodies, Bispecific); 0 (Immunoglobulin Fragments); 0 (Recombinant Protei

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16 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2001 ACS
AN 1992:5189 CAPLUS
DN 116:5189
TI Oligomeric monoclonal immunoglobulins for immunodiagnosis and therapy
IN Shuford, Walt W.; Harris, Linda J.; Raff, Howard V.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K035-14
ICS A61K039-00; A61K039-40; C12N005-02; C12N015-00
CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9106305	A1	19910516	WO 1990-US6426	19901106
	W: AU, CA, FI, JP, KR, NO				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	CA 2045150	AA	19910508	CA 1990-2045150	19901106
	AU 9170303	A1	19910531	AU 1991-70303	19901106
	AU 648056	B2	19940414		
	EP 462246	A1	19911227	EP 1991-901546	19901106
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 04505709	T2	19921008	JP 1991-501918	19901106
	NO 9102640	A	19910905	NO 1991-2640	19910705
PRAI	US 1989-432700	19891107			
	WO 1990-US6426	19901106			

AB Oligomeric monoclonal **antibodies** with high avidity for **antigen** are prepd. that have .gtoreq.2 Ig monomers assocd. together to form tetravalent or hexavalent Ig, esp. IgG. The oligomers are formed by substantially duplicating regions of the **light chain**, particularly the variable region. Oligomeric **antibodies** of the IgG isotype cross the placenta and can provide passive immunity to a fetus, which is particularly important for protecting newborns against, e.g. group B streptococci. A monoclonal antibody having a mol. wt. substantially greater than a typical IgG antibody was produced using V region genes cloned from the parental 4B9 lymphoblastoid cell line. The antibody (1B1 dimer) was specific for group B streptococcus, was 100-fold more active in an opsonophagocytic assay than the monomer, and passed through the placenta and into the fetus of rats. Rat pups treated with the antibody after i.p. injection of streptococci were protected at both low and high concns. of antibody. DNA sequences are shown for the 1B1 **light chain** and for chains of the 4B9 antibody.

ST oligomer monoclonal Ig diagnosis therapy; IgG oligomer Streptococcus newborn immunization; cloning IgG oligomer prodn

IT Mammal
(cell line of, oligomeric monoclonal Ig secretion by)

IT Phagocytosis
(enhancement of, with oligomeric monoclonal IgG)

IT Gene, animal
RL: PREP (Preparation)
(for Ig, cloning of, in prepn. of oligomeric monoclonal Ig for diagnosis and therapy)

IT Molecular cloning
(of genes for Ig, in prepn. of oligomeric monoclonal Ig for diagnosis and therapy)

IT **Polymerization**
(of monoclonal Ig, amino acid substitution for, in prodn. of oligomeric monoclonal Ig for immunodiagnosis and therapy)

IT Pharmaceutical dosage forms
(of oligomeric monoclonal IgG)

IT Animal cell line
(oligomeric monoclonal Ig secretion by)

IT Placenta
(oligomeric monoclonal Ig transport across, for passive immunization of fetus)

IT **Antigens**
RL: BIOL (Biological study)

(substitution of, in Ig **light chain**, in prodn. of oligomeric monoclonal Ig for immunodiagnosis and therapy)

IT Animal cell line
(4B9, oligomeric monoclonal Ig derived from)

IT Immunoglobulins
RL: PREP (Preparation)
(G, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)

IT Immunoglobulins
RL: PREP (Preparation)
(G1, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)

IT Immunoglobulins
RL: PREP (Preparation)
(G2, monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)

IT Immunoglobulins
RL: BIOL (Biological study)
(M, oligomeric monoclonal Ig derived from)

IT Embryo
(fetus, passive immunization of, with oligomeric monoclonal Ig)

IT Streptococcus
(group B, passive immunization against, in fetus and newborn, oligomeric monoclonal Ig for)

IT Therapeutics
(immuno-, oligomeric monoclonal Igs for)

IT Diagnosis
(immunol., oligomeric monoclonal Igs for)

IT Immunoglobulins
RL: PREP (Preparation)
(monoclonal, oligomeric, prodn. of, for immunodiagnosis and therapy)

IT Plasmid and Episome
(pN.gamma.1A2.1, heavy chain of oligomeric monoclonal IgG to group B streptococcus on, cloning and expression of)

IT Immunization
(passive, against streptococci, in fetus and newborn, oligomeric monoclonal Ig for)

IT 137067-93-7 137067-94-8
RL: PRP (Properties)
(amino-terminal sequence of recombinant light Ig chain of 1B1 monoclonal IgG)

IT 137748-88-0, Deoxyribonucleic acid (human clone 4B9-UK15 4B9 immunoglobulin G 1 **light chain** fragment-specifying) 137748-89-1, Deoxyribonucleic acid (human clone 4B9-UK15 immunoglobulin G 1 **light chain** fragment-specifying) 137749-00-9, Deoxyribonucleic acid (human clone pN.gamma.1A2.1 immunoglobulin G 1 heavy chain fragment-specifying) 137749-01-0, Deoxyribonucleic acid (human clone pNkA1.1 immunoglobulin G 1 **light chain** fragment-specifying)
RL: PRP (Properties)
(cloning and nucleotide sequence of)

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1980:530367 CAPLUS
DN 93:130367
TI In vitro studies of human seminal plasma allergy
AU Kooistra, J. B.; Yunginger, J. W.; Santrach, P. J.; Clark, J. W.
CS Dep. Med., Univ. Wisconsin, Madison, WI, USA
SO J. Allergy Clin. Immunol. (1980), 66(2), 148-54
CODEN: JACIBY; ISSN: 0091-6749
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB A 23-yr-old woman experienced generalized urticaria, angioedema, and respiratory obstruction after intercourse. Reactions increased in frequency and severity over a 2-yr period; sexual exposures were limited to her husband. Fresh, centrifuged seminal plasma samples from 4 donors, including her husband, evoked pos. immediate puncture skin-test reactions in dilns. of 1:100 or 1:1,000; no reactions were seen in normal control males. A borderline elevation in serum IgE antibodies to seminal plasma was noted by the radioallergosorbent test (RAST). However, the patient had elevated IgE antibodies to a partially purified seminal plasma fraction (IV) obtained by Sephadex G-200 gel filtration. Seminal plasma from all 4 donors showed similar allergenic activity when tested in fraction IV RAST inhibition expts. Further in vitro studies have characterized the allergenic components in fraction IV. Allergenic components (pool III) are distinct from acid phosphatase, have an apparent mol. **wt.** range from **20,000** to **30,**
000 daltons, produced multiple bands on isoelec.
focusing with isoelec. points of 6.6, 7.0, and 7.5, and produced multiple bands in polyacrylamide gel electrophoresis, indicating a heterogeneous group of antigens. Comparison of pool III with seminal vesicle secretions and prostatic homogenate via thin-layer isoelectrofocusing revealed protein bands which appeared to be common to all 3 materials. Thus, it remains uncertain as to whether allergenic proteins are derived from seminal vesicle or prostatic secretions. Condom usage by the patient's husband essentially prevented subsequent allergic reactions. However, serum IgE antibodies to fraction IV remained consistently elevated during a 28-mo follow-up period.
ST seminal plasma allergy; allergen seminal plasma characterization
IT Allergens
RL: PROC (Process)
(of seminal plasma, characterization of)
IT Allergy
(to seminal plasma protein)
IT **Immunoglobulins**
RL: BIOL (Biological study)
(E, to seminal plasma proteins)
IT Semen
(p

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1980:530367 CAPLUS
DN 93:130367
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AU Kooistra, J. B.; Yunginger, J. W.; Santrach, P. J.; Clark, J. W.
CS Dep. Med., Univ. Wisconsin, Madison, WI, USA
SO J. Allergy Clin. Immunol. (1980), 66(2), 148-54
CODEN: JACIBY; ISSN: 0091-6749
DT Journal
LA English
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000 daltons, produced multiple bands on isoelec.
focusing with isoelec. points of 6.6, 7.0, and 7.5, and produced multiple bands in polyacrylamide gel electrophoresis, indicating a heterogeneous group of antigens. Comparison of pool III with seminal vesicle secretions and prostatic homogenate via thin-layer isoelectrofocusing revealed protein bands which appeared to be common to all 3 materials. Thus, it remains uncertain as to whether allergenic proteins are derived from seminal vesicle or prostatic secretions. Condom usage by the patient's husband essentially prevented subsequent allergic reactions. However, serum IgE antibodies to fraction IV remained consistently elevated during a 28-mo follow-up period.
ST seminal plasma allergy; allergen seminal plasma characterization
IT Allergens
RL: PROC (Process)
(of seminal plasma, characterization of)
IT Allergy
(to seminal plasma protein)
IT **Immunoglobulins**
RL: BIOL (Biological study)
(E, to seminal plasma proteins)
IT Semen
(p

8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1980:424158 CAPLUS
DN 93:24158
TI Characterization of human lymphocyte surface receptors for mitogenic and non-mitogenic substances
AU Skoog, V. T.; Nilsson, S. F.; Weber, T. H.
CS Dep. Surg., Univ. Hosp., Uppsala, Swed.
SO Scand. J. Immunol. (1980), 11(4), 369-76
CODEN: SJIMAX; ISSN: 0300-9475
DT Journal
LA English
CC 15-2 (Immunochemistry)
AB To compare the receptor patterns for mitogenic and nonmitogenic substances, surface glycoproteins of human lymphocytes were labeled with the lactoperoxidase-catalyzed iodination technique and with a galactose oxidase-tritiated Na borohydride technique. Labeled cells were detergent-solubilized, and the lysates were allowed to react with insolubilized purified mitogenic lectins, phytohemagglutinin, leucoagglutinin, and an insolubilized nonmitogenic lectin, oxidized leucoagglutinin. Lectin-reactive proteins were eluted with Na dodecyl sulfate (SDS) buffer. Cell membrane components reactive with antilymphocyte globulin (ALG) were retrieved by indirect immunopptn. with protein-A-bearing staphylococcus Cowan I strain (SaCI). Lectin- and ALG-reactive proteins were analyzed by SDS polyacrylamide gel electrophoresis. Iodinated glycoproteins regularly showed 4 major components with mol. **wts**. of 120,000, 70,000, 60,000 and 43,000 **daltons**, resp., on 7% gels. An addnl. broad peak in the mol. **wt**. range **20,000**-35,000 **daltons** was found on 10% gels. Tritiated glycoproteins also showed 4 major components with mol. **wt**. 120,000, 70,000, 60,000 and 42,000, resp., which reacted with lectin and ALG. In addn., ALG reacted with some glycoproteins with mol. **wt**. between 150,000 and 230,000 **daltons**. On 10% gels addnl. lectin- and ALG-binding glycoproteins with mol. **wt**. around **30,000 daltons** were found. The similarity in structures bound by mitogenic and nonmitogenic substances indicates that lymphocyte activation may depend on some property conferred by the mitogen.
ST lymphocyte receptor mitogen **Ig**
IT Receptors
RL: PROC (Process)
(for mitogens, of lymphocytes, characterization of)
IT Glycoproteins
RL: BIOL (Biological study)
(of lymphocyte cell membrane, as receptors for mitogens)
IT Cell membrane
(of lymphocyte, glycoproteins of, as receptors for mitogens)
IT Glycoproteins
RL: BIOL (Biological study)
(of lymphocytes, as mitogen receptors rl)
IT Mitogens
(receptors for, of lymphocytes, characterization of)
IT Phytohemagglutinins
RL: BIOL (Biological study)
(receptors for, of lymphocytes, characterization of)
IT Lymphocyte
(rec